240 Exocrine pancreatic function and resting energy expenditure in Cystic Fibrosis

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The aim of this study was to prove the hypothesis that exocrine pancreatic function determines resting energy expenditure (REE) in Cystic Fibrosis (CF).
Thirty-eight CF individuals (9 to 34, 19.98±1.0 yrs) were divided in two groups: 32 patients, who had exocrine pancreatic insufficiency (PI) (Group A) and 6 patients with pancreatic sufficiency (PS) (Group B). A sub-group C included 19 PI patients whose predicted FEV1% was comparable to that of Group B. Indirect calorimetry and Schofield equations were applied to calculate predicted REE. Measured REE was expressed as % of the predicted values. BMI and BMI z-scores were related to REE.
The results were expressed as mean±standard error. Group A had increased REE% (113±3.81%) as opposed to group B whose REE% was similar to the predicted values (98.9±3.81%) ($p = 0.022$). Sub-group C also had increased REE% (110.82±2.72%), which was comparable to that of group A and significantly different from group B ($p = 0.035$). Mean FEV1% was 74.53±4.9%, 86.33±10.1% 92.1±4.55%, mean BMI was 19.7±0.5, 25.6±2.06 and 19.13±0.66 and BMI z-scores were −0.72±0.2, 0.75±0.51 and −0.62±0.26, in Group A, B and C, respectively. Significant correlation was demonstrated between REE% and BMI z-scores in-group B ($r = -0.83$, $p = 0.038$) but not in groups A and C.
Conclusions: Clinically stable CF patients with similar pulmonary function exhibited increased REE% only in the presence of exocrine pancreatic insufficiency. Pancreatic sufficiency was related to normal REE%. Furthermore, REE% strongly correlated with BMI z-scores in pancreatic sufficiency but not in pancreatic insufficiency. These findings support the hypothesis that exocrine pancreatic rather than pulmonary function may determine nutritional status and REE% in CF patients.

241 Exocrine pancreatic function evaluation in patients with Cystic Fibrosis and pancreatic sufficiency: a correlation study

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Background: Most patients with Cystic Fibrosis have pancreatic insufficiency (PI), however, 15% of the patients are pancreatic sufficient (PS). Many laboratory tests have been developed in order to examine exocrine pancreatic function to distinguish between PI and PS. The 'gold-standard' to determine pancreatic function apart from direct pancreatic stimulation test is the fecal fat excretion during 72 h, expressed as coeffiecient of fat absorption (CFA). Other tests include fecal elastase and serum immuno-reactive trypsinogen (IRT).Aim: To test the correlation between elastase and IRT as compared to fecal fat excretion, thereby, to evaluate the best available test to determine exocrine pancreatic function in CF patients.
Methods: 21 CF PS patients performed the 3 tests of fecal fat excretion, elastase and IRT. Correlation between the tests was evaluated by the kappa statistics test, sensitivity, specificity, positive and negative predictive values.
Results: The correlation between CFA and IRT was negative (kappa = −0.154), and between CFA and elastase was poor (kappa = 0.213). The sensitivity, specificity, positive and negative predictive values of IRT vs. CFA were: 0%, 88%, 0%, and 78%, respectively, and for elastase were: 40%, 81%, 40%, and 81% respectively.
Conclusion: Poor correlation was found between IRT, elastase and CFA, therefore, neither elastase in the stool nor IRT in the serum has the sensitivity or the specificity to replace the 'gold standard' test of fecal fat excretion during 72 h. Thus, despite the technical difficulties and the inconvenient of collecting stool, there is a need to evaluate precisely the pancreatic function of the CF patients, at least at the time of diagnosis, and non-infrequently during the follow-up period, especially when changes in clinical parameters occur.

242 Treatment with ALTU-135 results in a positive inverse relationship between coefficient of fat absorption with stool weight in subjects with Cystic Fibrosis-related pancreatic insufficiency

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Pancreatic insufficiency (PI) occurs in 89% of patients with cystic fibrosis (CF) and current therapy includes formulations derived from crude porcine extract. ALTU-135 is a microbially derived enzyme therapy incorporating novel cross-linking and protein crystallization technology to create highly purified, stable and potent enzymes.
Methods: Subjects ($n = 125$) were screened and randomized to one of three treatment arms of ALTU-135 for four weeks; Dose: Lipase/Protease/Amylase (Units USP/meal or snack): Arm 1: 5,000/5,000/750; Arm 2: 25,000/25,000/3,750; Arm 3: 100,000/100,000/15,000. During the treatment period, subjects were provided a controlled diet (100 g of fat/day) for 72 h, beginning and ending with a highly visible blue dye marker. Novel methodology using dye marker ensured a complete stool collection for determination of stool weight and coefficient of fat absorption (CFA).
Results: There was a significant difference between baseline and treatment stool weight ($p \leq 0.0001$) for all treatment groups. All treatment arms alone and in combination exhibited a significant inverse correlation between baseline stool weight and baseline CFA ($r = -0.7551$; $p < 0.0001$) and a significant inverse correlation between treatment stool weight and treatment CFA ($r = -0.7517$; $p < 0.0001$). There was also high correlation between the change in stool weight with the change in CFA ($r = -0.7283$; $p < 0.0001$).
Conclusions: ALTU-135 significantly decreases stool weight while improving CFA in patients with CF-related PI.

243 Enhanced coefficient of fat absorption using a novel pancreatic enzyme preparation, ALTU-135, with concomitant use of a proton pump inhibitor

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Background: A randomized double-blind parallel dose study of subjects ($n = 125$) with CF-related PI was conducted with a novel acid-stable microbially-derived pancreatic enzyme replacement therapy (ALTU-135) to determine the most effective dose to increase oral fat absorption on and off acid suppression.
Methods: Subjects were randomized to one of three treatment arms: Lipase/Protease/Amylase (Units USP/meal or snack)
Arm 1: 5,000/5,000/750
Arm 2: 25,000/25,000/3,750
Arm 3: 100,000/100,000/15,000
Subjects were stratified based on acid suppression use. Analysis of variance tested for differences in the treatment arm means for coefficient of fat absorption (CFA). Pairwise comparisons among treatment arms utilized Tukey's studentized range test.
Results: Proton pump inhibitors (PPIs) were associated with increased CFA response to ALTU-135 ($p = 0.0062$). No significant increases were observed in subjects receiving H2 receptor antagonists or antacids. Mean increases in CFA were higher for subjects on PPI versus subjects off: 10.0% v. −3.4%, 17.7% v. 8.4%, and 23.2% v. 15.1% for Arms 1, 2, and 3 respectively. This difference is significant at the lowest dose ($p = 0.007$) and approaches significance with Arms 2 and 3 combined ($p = 0.058$).
Conclusions: An acidic intestinal environment contributes to fat malabsorption by causing bile salt precipitation, which results in reduced lipid solubilization and lipolysis. Given the consistent activity of crystalline bacterial lipase in ALTU-135 across a wide range of pH, we believe that the use of a PPI improves the treatment effect of ALTU-135 by preventing bile salt precipitation.